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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,900	02/14/2002	David B. Weiner	UPAP-0497	3962

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COZEN O'CONNOR, P.C.
1900 MARKET STREET
PHILADELPHIA, PA 19103-3508

EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,900	WEINER ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,39-54 and 81-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16,39-54 and 81-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response submitted 6/4/04 have been entered. Claims 17-26, and 55-80 have been canceled. Claims 81-107 are newly added. Claims 15, 16, 39-54, and 81-107 are now pending in the application, and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 6/4/04 response would be addressed to the extent that they apply to current rejection.

Claim Objections

Claim 92 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 88. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15, 16, 39-54 stand rejected, and claims 81-107 are newly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, and 7 of U.S. Patent No. 6,348,449.

Newly submitted claims 81-107 are drawn to including cytokines in the nucleic acid molecule composition. The subject matter is fully disclosed in the cited patent (e.g. claim 9).

Applicants indicated that a terminal disclaimer will be filed upon identification of allowed subject matter. Until then the claims stand rejected for reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

The prior rejection of Claims 15-22, 24-26, 39-41, 45-47, 51, 55, 59, 60, 64, 68, 69, 73, 77 are rejected under 35 U.S.C. 102(e) as being anticipated by *Carson et al* (US 5,679,647, IDS/AK), is withdrawn in view of claim amendment.

Prior rejection of Claims 15-26 and 39-80 under 35 U.S.C. 102(f) is withdrawn because the application has the same inventive entity of the cited U.S. Patent No. 6,348,449.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejections under this provision have been modified in view of amendment.

Claims 15, 16, 39-41, 45-47, 51, 81, 83, 85, 87, 89, 93, 95, 99, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,679,647), in view of *Gately et al* (Cell Immunol 1992;143:127-42), and as evidenced by *Carson et al* (US 5,804,566) and the Webster's English Dictionary.

Carson et al ('647 patent) teach a method of inducing an immune response in an individual against an antigen by administering a plasmid vector (a nucleic acid molecule

free of an infectious agent) via mucosal route to mice, wherein the plasmid contains a DNA sequence encoding an influenza viral antigen operatively linked to a CMV promoter (regulatory sequence), which induced a humoral immune response (column 32, line 54 to column 33, line 14), and cellular immune response including antigen specific cytotoxic T lymphocytes (examples XII-XIV). *Carson et al* go on to teach that immunostimulatory *cytokine* could be co-administered with polynucleotides expressing an antigen to enhance the performance of the host immune system, particularly the helper and cytotoxic T lymphocytes (e.g. paragraph bridging columns 29-30). *Carson et al* teach that the mucosal routes of administration can be nasal, rectal, vaginal, urethra, or *mouth* topically (column 6, lines 21-27), and the principle is to deliver the naked DNA to areas rich in APC, such as the squamous mucosal epithelia of the buccal mucosa (column 6, lines 2-5). *Carson et al* also teach suppositors and topical preparations are suitable for mucosal administration (column 20, lines 11-19). *Carson et al* do not use the term "sublingual" in the '647 patent. However, the Webster's English dictionary defines "sublingual" as "SITUATED OR ADMINISTERED UNDER THE TONGUE", since the sublingual mucosal occupies majority of the mucosal area of the mouth, the term "mouth" is a reasonable alternative for "sublingual". In the '566 patent, *Carson et al* listed the sublingual means of delivery along with the oral, inhalation, and nasal routes in the same Markush group, and thus evidenced the sublingual injection is a well-known route for mucosal antigen delivery (column 20, line 46). *Carson et al* do not teach using IL-12 as the immunostimulatory molecule.

Gately et al supplemented the teaching of *Carson et al* by establishing that it is well known in the art that IL-12 is a cytokine that could enhance the performance of activated T lymphocytes and natural killer cells, which are immune cells particularly relevant to host defense against pathogens such as viruses. *Gately et al* teach that IL-12 could stimulate LAK cells as well as CTL responses, thus useful as a therapeutic agent against tumors and infectious diseases (e.g. abstract and introduction).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Carson et al* with that of *Gately et al* by simply selecting one of the art known routes of antigen administration, such as buccal or sublingual for vaccination and including IL-12 in the vaccine composition with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because in light of numerous art known mucosal delivery routes and immunostimulatory cytokines, these limitations would fall within the bounds of the optimization. Further, given the success disclosed in the individual references, the reasonable skilled would have had a reasonable expectation of success when use them combined. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

In the 6/4/04 response, applicants argue that the '647 patent conspicuously omits sublingual as a route of administration, and when taken in combination with '566 patent, one would conclude that sublingual is not among the acceptable mucosal routes of delivery.

In response, *Carson et al* '647 patent provides a long list of mucosal tissue specific routes of administration, i.e. nasal, rectal, vaginal, urethra, buccal, or mouth topically (column 6, lines 21-27), and teach that the principle for selecting a proper route is to deliver the naked DNA to areas rich in APC, such as the squamous mucosal epithelia of the buccal mucosa (column 6, lines 2-5). Although they do not use the term "sublingual", it is well known in the art such as defined in the Webster's English dictionary for sublingual, "situated or administered under the tongue", which takes majority of the mucosa in the mouth. The Office does not consider the choice of words for describing the mucosal specific routes was conspicuous in the absence of evidence to the contrary.

Applicants then assert that the combined teachings of the '647 and '566 patents teach away from instantly claimed invention without given particular explanation.

A closer look of the '566 patent, *Carson et al* refer to the sublingual route along with the nasal, oral, and inhalation. *Carson et al* did mention a less successful experience in suppressing IgE antibody response for the allergen tolerance regimen when using the mucosal routes compared to the intradermal route. However, the discussion does not negate the sublingual route as one of the mucosal routes of nuclei acid delivery, it only suggests the allergen tolerance regimen was not ideal using mucosal route as a whole. Further, the regimen still achieved certain degree of success even though it is less effective compared to the intradermal route. Accordingly, the combined teachings of the '647 and '566 patents do not teach away from instantly claimed invention.

Claims 42, 43, 48, 49, 52, 53, 90, 91, 96, 97, 102, 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Carson et al* (US 5,679,647 and 5,804,566), and *Gately et al* (Cell Immunol 1992;143:127-42) as applied to claims 15, 16, 39-41, 45-47, 51, 81, 83, 85, 87, 89, 93, 95, 99, 101 above, further in view of *Wang et al* (PNAS 1993;90:4156-60).

The teachings of *Carson et al* and *Gately et al* disclosed a method for inducing immune response against a viral antigen, preferably combined with an immunostimulatory cytokine such as IL-12 as discussed in detail above. However, the combined teachings do not specifically define that the antigen is from human immunodeficiency virus, preferably comprises an epitope of gp160.

Wang et al supplemented the teachings of Carson et al and Gately et al by establishing that it is known in the art at the time of instant filing date, one could administer HIV gp160 for vaccine purpose. *Wang et al* teach administering a plasmid encoding an HIV gp160 as vaccine for HIV infection, and induced both humoral and cellular immune response via intramuscular injection. *Wang et al* do not teach the mucosal route of administration. However, *Carson et al* teach the advantage of using mucosal administration over intramuscular administration, "ROUTES OF ADMINISTRATION OF NAKED POLYNUCLEOTIDES THROUGH SKIN OR MUCOSA REQUIRE A LOWER CONCENTRATION OF DNA TO PRODUCE THE SAME MAGNITUDE OF IMMUNE RESPONSE THAN DOES THE INTRAMUSCULAR ROUTE OF ADMINISTRATION", and this is particularly desirable when using the DNA introducing a foreign antigen (column 8, lines 30-44).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the methods taught by *Carson et al, Gately et al,* and *Wang et al* for developing vaccine against an antigen of interest such as the HIVgp160 with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the mucosal route requires less amount of antigen for inducing an effective immune response and it is within the knowledge of the skill to select the antigen of interest for vaccination. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Applicants argue that Carson et al neither discloses nor suggests sublingual administration. This argument has been addressed in the above rejection, thus will not reiterate here.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the drawings on record are hand-written informal drawings. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Q. Janice Li
Primary Patent Examiner
Art Unit 1632

QL
August 16, 2004